

SPL Process ER/DL Meeting Meeting Minutes Jan 11, 2017 With FDA responses (Jan 31, 2017)

Chair of today's meeting: Pat Cowall

Teleconference information:

USA Toll-Free: 866-213-2145

USA Paid/International: 609-454-9913

Access code: 273 8216

Link to the SPL wiki:

<http://spl-work-group.wikispaces.com/share/view/51351516>

Agenda:

1. Questions/responses from Minutes of Oct 19 meeting – FDA presentation on Final Rule and Common Errors (minutes sent out in separate email and will be posted on the wiki)
 - a. Maricarmen Dilone-Rapaso: Discuss Listings obligation for manufacturer in both functions its own products and for Private Label Distributor

Team Discussion:

Pat: As a PLD manufacturer, the establishment has to drug list as the manufacturer using its own labeler code and make sure that the PLD drug listing is completed using the PLD labeler's code.

Howard: We have seen products manufactured by a CMO that use the manufacturer's labeler code, instead of the PLD. What is going on?

Response: This is not consistent with the Final Rule. These situations will hopefully be corrected with the implementation of the final rule with more specific instructions.

- b. Trish Pasek: In regards to Q12. Listing requirements for manufactures who make the same product for multiple PLDs
Based on the FDA's Response, the manufacturer must list using their own NDC... we assume, if the manufacturer does not plan to commercial market in their own labeling under their own NDC, the marketing start date would be a future date. Is this how everyone else interprets this?

Team Discussion:

A mfg exclusively for PLD listing should be created for your manufacturing listing. You are supposed to use the manufacturing start date as the start date in the manufacturing listing.

You need to put an image of the representative label in for the PLD, even though it may differ for the each PLD.

If a CMO markets a product itself (ie under its own labeler code), then there should be 2 drug listings:

- The normal product drug listing with COL (ie that the CM is marketing).
- The "mfg exclusively for PLD" drug listing with no COL and image of label.

- c. Trish Pasek: In regards to Q17. Can NDCs be reused if it's the same pkg for that product that comes back into the market (everything is the same as far as the ingredients of the product)? Based on the FDA's Response, this is completely understood, however, my question/concern – If the market end date is removed and resubmitted to the Agency because it is not back on the market, will this affect the ability of CMS to know the point in time the product was OFF the market for claim purposes? Maybe we aren't concerned with this, just curious.

Team Discussion:

Comment: In this situation, one company has removed the market end date....and he hasn't had any issues in the past

Questions to FDA:

1. Are you supposed to remove the market end date (using the original market start date)....or put in a new market start date (representing the date that marketing was resumed) with no market end date?
2. Do you keep a history of all the start/end periods....for CMS payment purposes... so third party payers know all the active and inactive time periods for the product?
Or
Do you just record one continuous marketing period.

Concern: CMS and 3rd party payers would not be responsible for reimbursements during the inactive period. Therefore it is important to be able to keep track of the inactive periods so that there are no issues with reimbursement.

FDA response:

There is nothing specifically written in the regs about this situation. They have seen companies do both, and both are acceptable.

Recommendation:

The DRLS staff has determined that the original Marketing Start Date should be used (left in place) when a product with the same NDC is re-activated. This applies to packaging marketing Start dates as well. A package NDC that is dropped or discontinued should be reactivated using the original Marketing Start Date if that data element is provided.

The FDA feels that it would be misleading for a product to change Marketing Start Dates, and it is more important and meaningful to FDA to maintain the original date of introduction into the market.

As for reimbursement issues, that is really up to CMS procedures and such a question should be posed to CMS. However, we note that products which are discontinued are updated as such on the NDC Directory, the NSDE file, and at DailyMed. So, if a reimbursement request is received for something that is currently off the market, a check to any of these files should reflect that status.

- d. Trish Pasek: In regards to Q19. Is a new NDC product code required by the private label distributor for a change in manufacturer?
The FDA's response is alarming to me since only one set id is allowed for the same NDC. If a private label distributor, who assigns their own NDCs, has multiple manufactures, each required to drug list their manufactured product using the PLDs NDC, ONLY the first manufacturer to list WILL be successful. All others will receive a validation error pertaining to the set id and NDC.

Team Discussion:

Example for discussion:

PLD had assigned an NDC to the product. They use 2 suppliers (CMOs) A and B.

- Supplier A. Supplier A manufactures the product and initially drug lists the product.
- Supplier B. PLD is now adding supplier B for the product. PLD told supplier B to use the same NDC code.
- Issue: Supplier B got validation issues when they submitted the SPL ----- because they couldn't submit the same NDC in an SPL file with a different set ID.

Note: Manufacturers are responsible for drug listing the products, not the PLD.

Resolution options:

- Option 1: Supplier B should tell the PLD to have Supplier A include Supplier B in Supplier A's drug listing SPL file. Issues:
 - Supplier A doesn't want to include Supplier B in their listing. They are only responsible for their own work.
 - Supplier B would have to assure that Supplier A actually does it. However, mfg information can be redacted so they can't review the SPL. Practically, this can't be done because the communication will never happen!!!
- Option 2: Supplier B can drug list the product using a different NDC code (using the PLD labeler code).

Another hint: To make sure that you don't have any issues with the NDC they plan to use: CMOs should drug the product as soon as they know they are going to make the product (even before they start mfg'ing it) to lock down the NDC code.

Questions to FDA:

Option 1 does not seem practical for Supplier B. How did you envision this working when you gave the answer to Q19?

Also, this also doesn't work well when a PLD switches suppliers. Supplier A's SPL has to remain active until the last lot expires. And Supplier A doesn't have any incentive to turn over their SPL file to Supplier B. Any ideas on how to make this work?

FDA response:

The same NDC can be used if all the product characteristics are the same – including imprint, color, size, shape, or labeling. If there is any difference from supplier A than Supplier B, then a new NDC should be assigned. A company is not prevented from assigning different NDCs for the different manufacturers.

FDA understands the concern, and this should be worked out between the PLD and the supplier. If the PLD wants to use the same NDC number, the PLD can do their own drug listing.

- e. If a domestic CMO markets a product and also manufactures it for a PLD, what are the CMO's listing requirements? We know we have to create:
 - CMO: Complete drug listing for their own product
 - PLD: Complete drug listing for the PLD product
 - Question: Does the CMO have to do a "Mfg exclusively for PLD"? If so, how do they plan to enforce this, because the product is not going to go through customs.

FDA response:

The CMO would have to do a Mfg exclusively.... ONLY if there is a difference between the products that they manufacture (these differences would potentially include the color, imprint, etc).

Topics for the Next Meeting- Feb 8 or 22

- 2. Draft Guidance on Submitting Manufacturing Establishment Information -- Basic introduction from initial reading of the draft guidance.

Lonnie is coming to the meeting on Feb 8th to discuss the new SPL document type.

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM534709.pdf>

Team Discussion:

Background (courtesy of Gary Saner's email to the tech team):

On Dec 28, 2016, the FDA posted a Draft Guidance on **Providing Regulatory Submissions in Electronic Format—Submission of Manufacturing Establishment Information**

Problem: Manufacturing Establishment Information (MEI) is often provided in different sections throughout a drug or biologic application. "This makes the MEI difficult to find and time-consuming to review. Consolidating the required electronic MEI to appear in a single location will facilitate the complete, timely, and accurate review of all manufacturing establishments..."

Solution/Requirement: MEI data must be captured electronically in SPL format and submitted in New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), Biologics License Applications (BLAs), and Amendments, Supplements, or Resubmissions of these application types and related Drug Master Files (DMFs).

Plans: FDA plans to create a new, dedicated SPL Doc Type for this MEI file. The FDA SPL Implementation Guide is expected to be updated soon to define the details. The SPL-MEI document is expected to be similar, but different than the existing SPL-ER document used for actual establishment registration.

Effective Date: 24 months after the Final GFI is published

Here is [summary](#) from RAPS of the recent [draft guidance](#) on submission of manufacturing establishment information (MEI) in electronic format. My detailed summary is below:

- Implementation 24 months after final guidance issued so we have at least 2+ years until this requirement goes into effect.
- This impacts NDAs, BLAs, ANDAs and supplements/amendments/annual reports impacting these submissions.
 - Non-commercial INDs are explicitly excluded from these requirements, but no mention of commercial INDs is made. This is odd because other recent electronic submission format guidance documents have included commercial INDs. Need to wait for final guidance for further clarity.
- The information from 3.2.S.2.1 and 3.2.P.3.1 must be consolidated in a new file located in 3.2.R in HL7 Version 3: SPL format.
 - The current files in 3.2.S.2.1 and 3.2.P.3.1 must be replaced with a link to 3.2.R. No other files can be submitted in 3.2.S.2.1 and 3.2.P.3.1.
 - The file in 3.2.R must be named “establishment-information-[Date of the submission (YYYY-MM-DD)].xml” and the leaf title must be “Establishment-Information-[Date of the submission (YYYY-MM-DD0)].”
- MEI encompasses:
 - Establishment name and address: Specific information regarding the physical location
 - Unique Facility Identifier (separate [guidance](#) indicates this is DUNS number)
 - Contact information for the person responsible for scheduling inspections
 - Specific manufacturing operations being conducted
 - FEI number (recommended but not required)
- MEI must include complete information for all manufacturing sites such as:
 - Manufacturing sites
 - Packaging sites
 - Labeling sites
 - Testing sites (both for routine batch testing and stability testing)
 - There are no waivers to this requirement

Document	Product	Establishment	Estab. Business Operations	Estab. Regulatory Contact	Estab. Inspection Contact
Marketing Authorization (eCTD)	X	X (currently scattered)	X		
Drug Establishment Reg. (SPL-ER)		X	X	X	
Drug Listing (SPL-Listing)	X	X	X		

Discussions at future SPL meetings:

Mark your calendars... Lonnie Smith is planning to come to several SPL team meetings to discuss the new FDA MEI Draft Guidance and changes to the SPL Implementation Guide

- SPL ER/DL meeting on Feb 22nd, 1-2 PM ET (date uncertain)
- SPL Tech Team meeting on Feb 13, 2:00-3:00 PM ET. (date uncertain)

3. Trish Pasek: For those of you who manufacture OTC products for multiple PLDs, have you been contacted by them regarding NDCs that have been registered for their labeling? Additionally, for those who may distribute under another manufacturers application, such as an ANDA, have you been contacted by the owner of that application to provide all NDCs commercially marketed under that application? (more out of curiosity)

Team Discussion:

4. Other walk ins.

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